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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,606	11/13/2006	Robert L. Fine	68074-A-PCT-US/JPW/CH	4899

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COOPER & DUNHAM, LLP
30 Rockefeller Plaza
20th Floor
NEW YORK, NY 10112

EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,606	FINE ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,23,26-28,31,36 and 37* is/are pending in the application.

4a) Of the above claim(s) *26-28 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,23,31 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I (claims 1-20, 23 and 36) in the reply filed on 11/3/2008 is acknowledged. The traversal is on the ground(s) that lack novelty or inventive step of group I over US patent 5527676 and lack of unity of inventions group I-III and group I and IV are not established.

These have been considered. Applicant's argument on that the claimed peptide (SEQ ID NO: 1 linked to SEQ ID NO: 2) is novel over the p53 sequence disclosed by Vogelstein et al., (US Patent 5527676) alone is accepted.

Under the PCT rule 13.2 unity lacking is because claimed molecules do not share a common property or activity or the same or corresponding technical feature including the claimed product, method of making the product, and first method of using the product. Group II is drawn to a DNA comprising the DNA encoding the peptide of claim 1 plus a plasmid having a viral vector that is not included in the peptide of claim 1, therefore, there is no same technical feature (property and activity of virus). Therefore the unity between invention group I and II is lacking.

Since invention group III, drawn to a method of treating a cancer patient by administering the peptide of claim 1, is the first method of using the peptide of claim I, group III will be rejoined with group I for examination in this action.

Group IV is not the first method of using the peptide of claim 1, therefore, there is no unity between invention group I and IV.

For the reasons above, group III and I are together examined and the rest parts of the requirement are still deemed proper and is therefore made **FINAL.**

Claims 1-20, 23, 26-28, 31, and 36-37 are pending.

Claims 26-28, and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim.

Claims 1-20, 23, 31 and 36, drawn to a polypeptide comprising SEQ ID NO: 1 linked to its palindrome showing in SEQ ID NO: 2 as dimers or a tetramer and a method of treating cancer with the peptide of claim 1, are examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 10/9/2007 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquires set forth in Graham V. john Deere Co., 383 U.S. 1, 148 USPQ 459 (1996), that are applied for establishing a background for determining obviousness under 25 U.S. 103 (a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-3, 7-10, 14, 15, 19-20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al (PNAS vol 92, page 9455-9459, 1995) in view of Hoffman et al (US Patent No 5545727, issues 1996) as evidenced by sequence search result.

Claims are drawn to a polypeptide comprising a first segment of continuous amino acids having the sequence of AQAGKEPGGSRAHSSHLKSKKGQSTSRHKKLMFKTEGPDSD (SEQ ID NO: 1 covalently linked to a second segment of continuous amino acids having the sequence of DSDPGETKFMLKKHRSTSQGKKSKLHSSHARSGGPEKGAQA (SEQ ID NO: 2).

The sequence search result shows that SEQ ID NO: 1 is 41 amino acid peptide of C-terminal fragment of p53 protein (393 amino acids) at position 353-393 (see attached).

SEQ ID NO: 2 is palindrome of SEQ ID NO: 1. Thus claims are drawn to a polypeptide comprising a dimer or a tetramer of SEQ ID NO: 1 linked at different ends of the sequence such as 5'-3'--linking--3'-5' or 3'-5'-linking—5'-3' etc.

The claimed tetramer (SEQ ID NO: 5, 6, or 7) comprise two dimers (SEQ ID NO: 3 or 4) linked with or without glycine as a single linker.

Reed et al., teach that C-terminal segment of p53 is responsible for DNA binding of p53 protein and its activities. Reed et al., teach the functional domain of p53 forms dimers or a stable tetramer to bind DNA (page 9456, and page 9459, figure 4). Reed et al., further teach that the C-terminal segment contains amino acids 318-393 of human p53 protein, which comprises the 41 amino acids of SEQ ID NO: 1(page 9456, col 2, last line and fig 1, search result). SEQ ID NO: 2 is the palindrome of SEQ ID NO: 1. Reed et al., also teach that six histidine tag attached to the N-terminus of the p53 segment of p53 for purification (page 9455, col 2). Reed et al., also suggest that the dimer or tetramer is formed as mirror structure (figure 4), i.e. dimer comprised in the tetramer would be formed by linking the sequence of SEQ ID NO: 1 to its palindrome sequence of SEQ ID NO: 2 as 5'-3' --linking--5'-3', that is equal or the same to a peptide formed by linking two SEQ ID NO:1 as 5'-3'--linking--3'-5'.

Reed et al., do not teach that the peptides of dimers or tetramer are covalently linked by a single glycine linker.

Hoffman et al., teach a method of making a fusion protein or multimers by cross linking or covalently linked by a single glycine linker and teach the advantage of glycine(s) as a linker including the flexibility, stability, and sensitivity to the enzyme digestion (col 34+ and example 26).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to make dimers or a tetramer (SEQ ID NO: 3-7) of a C-terminal segment of p53 comprising the amino acids of SEQ ID NO: 1 and/or its palindrome of SEQ ID NO: 2. One of ordinary skill in the art at the time the invention

was made would have been motivated to modify the multimer peptide of Reed by cross-linking or covalently linked without or with a single glycine as taught by Hoffman et al., in order to use the polypeptide for cancer treatment because delivering a multimer peptide in the physical condition would disassociate the peptide complexes bound by affinity, not chemically linked. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success to make a tetramer comprising two dimers with a segment of p53 comprising SEQ ID NO: 1 or its palindrome because Reed et al., have shown the C-terminal segment of p53 (318-393) forming a tetramer to function as DNA binding protein in the DNA transcription or damage and Hoffman et al have shown a method of making a multimer by single glycine as a linker. Thus, the references in combination teach every limitation of the claims and the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

2. Claims 1, 4-9, 11-14, 16-18, 31 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed et al., (PNAS vol 92, page 9455-9459, 1995) in view of Hoffman et al., (US Patent No 5545727, issues 1996) as evidence by sequence search result as applied to claims 1, 7-9, and 14 above, and further in view of Pincus, M. WO2003/105880, filing March 2003, priority to March 2002, Published Dec. 2003).

The claims are set forth above, wherein the peptide further comprising a membrane carrier peptide attached to the C-terminus of the peptide and pharmaceutical composition for treating a cancer.

Claim 31 is drawn to a method of treating a cancer by administering the peptide of claim 1.

The teaching of Reed and Hoffman et al are set forth above. Read et al further suggest that the tetramerization of p53 C-terminus regulates p53 function as a tumor suppressor protein.

Reed and Hoffman et al do not teach dimer or tetramer peptide further comprising a carrier protein or peptide from Antennapedia having amino acids of SEQ ID NO: 8 and make a pharmaceutical composition for treating a cancer.

Pincus M. teaches a membrane penetrating leader sequence (KKWKMRRNQFWVKVQRG) that is identical to the amino acid sequence of SEQ ID NO: 8 (page 3, line 3 from bottom). Pincus M. teaches that the membrane penetrating leader sequence is fused to the C-terminus of fusion polypeptide comprising a fragment of p53 (page 5, line 9-10) and teaches a pharmaceutical composition comprising the fusion peptide for killing human cancer cells or treating a cancer patient.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to fuse the carrier peptide comprising the leader sequence of SEQ ID NO: 8 to the dimers or the tetramer (SEQ ID NO: 3-7) of the c-terminal segment of p53 comprising the amino acids of SEQ ID NO: 1 and/or its palindrome of SEQ ID NO: 2 with expected result. One of ordinary skill in the art at the time the invention was made would have been motivated to modify the multimer peptide of Reed and Hoffman et al., by adding the membrane penetrating peptide in order to administrate the polypeptide to human or cells for cancer treatment because delivering

a multimer peptide in biological or physical condition would disassociate the peptides bound by affinity and because the polypeptide has a large molecular weight, which would required a carrier protein to transport into the a cell or nucleus for function. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success to link the carrier peptide to the dimers or tetramer and form a pharmaceutical composition and administering the peptide for treating cancer because Reed et al., have shown the C-terminal segment of p53 functions as a tetramer for p53's function, Hoffman et al have shown a method of making multimer by single glycine as a linker and Pincus teaches the carrier peptide of SEQ ID NO: 8 and a fusion protein comprising p53 fragment for treating a cancer. Thus, the references in combination teach each and every limitation of the claims and the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643